UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,801	09/10/2003	Paolo Gatti	PC23575A	1817

28940 7590 06/27/2007

PFIZER INC
10555 SCIENCE CENTER DRIVE
SAN DIEGO, CA 92121

EXAMINER	
SCHLIENTZ, NATHAN W	
ART UNIT	**PAPER NUMBER**
1616	

MAIL DATE	DELIVERY MODE
06/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,801	GATTI, PAOLO	
	Examiner	Art Unit	
	Nathan W. Schlientz	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *107 and 110-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *107 and 110-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/11/04 and 6/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner for your application in the USPTO has changed. Examiner Nathan Schlientz can be reached at 571-272-9924.

Status of Claims

Claims 108-109 have been cancelled in an amendment filed in conjunction with a Request for Continued Examination on 1 February 2007. As a result, Claims 107 and 110-119 are pending and examined herein on the merits for patentability. No claim is allowed at this time.

Claim Objections

1. Claims 110, 112, 118 and 119 are objected to because of the following informalities: Claims 118 and 119 are duplicates of Claims 110 and 112, respectively. Claims 110 and 118 comprise 40 wt.% 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide L-malate, 47.5 wt.% mannitol, 6 wt.% croscarmellose sodium, 5 wt.% povidone and 1.5 wt.% magnesium stearate, which totals to 100 wt.%. Claims 112 and 119 comprise 15.2 wt.% 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide L-malate, 72.7 wt.% mannitol, 6 wt.% croscarmellose sodium, 5.1 wt.% povidone and 1 wt.% magnesium stearate, which totals to 100 wt.%. Therefore, neither sets of claims can comprise any additional

components, and thus the respective sets are exactly the same. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. The rejection of Claims 107-119 under 35 U.S.C. 102(b) as being anticipated by International Application Publication WO 01/37820 (hereinafter Shenoy et al.) is hereby withdrawn by the examiner in view of Shenoy et al. not explicitly disclosing the L-malate salt of 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. The rejection of Claim 117 under 35 U.S.C. 103(a) as being unpatentable over Shenoy et al. in view of U.S. Patent Application Publication No. 2003/0069298 (hereinafter Hawley et al.) is hereby withdrawn by the examiner in light of the fact that the subject matter of Hawley et al. and the instant application were owned by the same assignee at the time of the instantly claimed invention (MPEP 706.02(1)(3)).

2. Claims 107 and 110-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shenoy et al.

Applicant claims:

Claim 107 is drawn to a solid formulation comprising 35-45 wt.% of 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide L-malate, 10-86 wt.% diluent (i.e. mannitol), 2-20 wt.% binder (i.e. croscarmellose sodium), 2-20 wt.% disintegrant (i.e. povidone), and 1-10 wt.% lubricant (i.e. magnesium stearate), wherein the formulation does not comprise a surfactant or a flow enhancer.

Claims 110 and 118 are drawn to a solid formulation comprising 40 wt.% 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide L-malate, 47.5 wt.% mannitol, 6 wt.% croscarmellose sodium, 5 wt.% povidone and 1.5 wt.% magnesium stearate.

Claim 111 is drawn to a solid formulation comprising 10-16 wt.% 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide L-malate, 65-80 wt.% mannitol, 5-10 wt.% croscarmellose sodium, 4-8 wt.% povidone and 1-2 wt.% magnesium stearate.

Claims 112 and 119 are drawn to a solid formulation comprising 15.2 wt.% 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide L-malate, 72.7 wt.% mannitol, 6 wt.% croscarmellose sodium, 5.1 wt.% povidone and 1 wt.% magnesium stearate.

Claim 113 is drawn to the formulation of Claim 107, wherein the formulation does not comprise a surfactant or flow enhancer.

Claims 114-116 are drawn to the bulk density of the formulation.

Claim 117 is drawn to the particle size of the solid formulation of Claim 107.

Determination of the scope and content of the prior art

(MPEP 2141.01)

With respect to Claim 111, Shenoy et al. teach a formulation comprising 0.01-***10*** wt.% ionizable substituted indolinone, 10-***80*** wt.% diluent, 0-***5*** wt.% binder, ***4***-10 wt.% disintegrant, and ***1***-1.5 wt.% lubricant (pages 92 and 93, Table: "All formulation components") (***emphasis added***).

With respect to Claims 107, 110 and 112-119, Shenoy et al. teach a formulation comprising 15-75 wt.% ionizable substituted indolinone, 5-95 wt.% binder, 4-10 wt.% disintegrant, and 1-1.5 wt.% lubricant (page 96, 2nd Table, "Indolinone + Surfactant + Diluent + Binder + Disintegrant + Lubricant + Flow Enhancer").

Shenoy et al. further teach that 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide is a suitable ionizable substituted indolinone (page 39, compound 80; and pages 158-159, Example 80). Shenoy et al. also teach that the ionizable substituted indolinone contemplated for use are pharmaceutically acceptable salts which do not abrogate the biological activity and properties of the compound (page 60, lines 1-6), wherein the ionizable substituted indolinone is reacted with a molar equivalent of a base solution or an acid solution, such as malic acid (page 65, lines 1-4; page 76, lines 1-3).

Shenoy et al. also teach suitable pharmaceutically acceptable diluents include mannitol (page 73, lines 14-15); suitable pharmaceutically acceptable binders include polyvinylpyrrolidone (i.e. povidone) (page 73, lines 17-18); suitable pharmaceutically acceptable disintegrants include crosscarmellose (page 73, lines 19-21); suitable pharmaceutically acceptable lubricants include magnesium stearate (page 73, lines 26-27).

With respect to Claim 113, Shenoy et al. teach that the broadest range of surfactants and flow enhancers encompasses 0 wt.% (pages 92 and 93, Table: "All formulation components"; and page 96, 2nd Table, "Indolinone + Surfactant + Diluent + Binder + Disintegrant + Lubricant + Flow Enhancer").

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Although Shenoy et al. teach 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide

as a suitable ionizable substituted indolinone, and the acid solution comprising malic acid, Shenoy et al. do not explicitly teach the L-malate salt of 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide. However, it is well-known in the art at the time of the instant invention to employ pharmaceutically acceptable salts of compounds in pharmaceutical formulations in order to enhance the solubility of the compound, thus providing greater solubility. Shenoy et al. teach that salts tend to be more soluble in aqueous or other protonic solvents than are corresponding free base forms (page 87, lines 8-12).

With respect to claims 114-117 of the instant application, absent a showing to the contrary, since the instantly claimed formulations are obvious over Shenoy et al., the prior art compositions would inherently possess physicochemical properties (i.e., bulk density and particle sizes) that are identical to those claimed in Claims 114-117. As a result, Shenoy et al. anticipate said claims.

As a practical matter, the USPTO is not equipped with the scientific laboratory instrumentation and facilities necessary for the manufacture of the myriad of claimed products set forth before it and then obtain requisite prior art products so as to conduct side-by-side analytical comparisons of the physicochemical properties inherently associated therewith. See *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Powder Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new

function or unknown property, which is inherently present in the prior art, does not necessarily make the claim patentable. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); and MPEP § 2112. Furthermore "products of identical chemical composition can not have mutually exclusive properties," since a chemical composition and its properties are inseparable. See *In re Spada*, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990); and MPEP § 2112. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. See MPEP § 2112.

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one skilled in the art at the time of the invention to use the L-malate salt of 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide in the formulations of Shenoy et al. because Shenoy et al. reasonably teach 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide as a suitable ionizable substituted indolinone and that salts tend to be more soluble in aqueous or other protonic solvents than are corresponding free base forms.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to

one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

1. Applicant's arguments, see pages 4-6, filed 1 February 2007, with respect to the rejection of Claims 107-119 under 35 USC 102(b) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new grounds of rejections are made, as detailed above.

2. Applicant's arguments, see page 8, filed 1 February 2007, with respect to the rejection of Claim 117 under 35 USC 103(a) as being unpatentable over Shenoy et al. in view of Hawley et al. have been fully considered and are persuasive. The rejection of Claim 117 has been withdrawn.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan W. Schlientz whose telephone number is 571-272-9924. The examiner can normally be reached on 8:30 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nathan W. Schlientz
Patent Examiner
Technology Center 1600
Group Art Unit 1616

Johann R. Richter
Supervisory Patent Examiner
Technology Center 1600
Group Art Unit 1616